

Key points

Lancet Paper: Importance of Background Rates of Disease in Assessment of Vaccine Safety

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- On Saturday, October 31st, 2009, a scientific publication and companion editorial in the journal *The Lancet* will be published that discusses background rates of numerous adverse events for several countries.
- Adverse events—such as sudden deaths, spontaneous abortions, and Guillain-Barré syndrome—will occur in the population. These will occur whether or not people have been vaccinated. In the context of vaccine safety monitoring, we call these naturally occurring events “background rates.”
- Several countries have begun mass vaccination campaigns to combat the 2009 H1N1 virus. Awareness of the background rates of several adverse events is critical to assessing the safety of the vaccine. This information allows public health and medical experts to identify when adverse events are occurring more frequently than would be expected in the absence of vaccination and need more detailed investigation to determine if the vaccine is causing the adverse events.

Benefits of background rate analysis

- Background rates are helpful as a tool to assess vaccine safety by comparing the expected rate of adverse events to the actual/observed rate in any given timeframe once vaccination begins.
- Some clustering – a number of cases in a limited timeframe or area – of adverse events occurs normally, and we can expect this clustering to continue during the period that 2009 H1N1 vaccinations are given.
- By comparing the expected rate of adverse events to the actual/observed rate in any given timeframe, we can put adverse event reports in proper context.

Limitations of background rate analysis

- Background rates can vary widely by location, age, sex and ethnicity, and therefore these factors should be considered when using background rates to compare events that occur following vaccination.
- Background rates by themselves usually are not sufficient as a way to fully assess vaccine safety. Full analysis requires review of individual reports and carefully controlled epidemiologic study.

Enhanced Vaccine Safety Surveillance

- Background rates are one piece of the puzzle. The current extensive US and international safety monitoring systems, activities and collaborations represent an unprecedented commitment to ensuring the safety of the 2009 H1N1 vaccines, as well as a model for how we might improve assessment of safety for all vaccines going forward.
- To use background rate estimates to understand whether health events are increasing when vaccines are used, continuous monitoring of both vaccination coverage and many health events is needed. Several countries have enhanced vaccine safety monitoring efforts. For example, in the United States:
 - The Vaccine Adverse Event Reporting System (VAERS) is a voluntary reporting system that identifies potential vaccine safety signals: healthcare providers are actively reminded to report suspected issues, and medical personnel are conducting daily reviews and follow-up [<http://vaers.hhs.gov>].
 - Second, a new Web-based active surveillance system is being implemented to prospectively follow tens of thousands of vaccinated people [www.myflushot.org].
 - Third, large population-based systems that link computerized vaccination data with healthcare codes will be used to conduct rapid and ongoing analyses. This approach includes data from large managed care plans, other health plans, Department of Defense, Medicare and the Veterans' Administration.
 - Fourth, active case finding for GBS is being conducted in 10 areas of the United States (a combined population of about 50 million people).
 - Findings from all sources are cross-referenced and reviewed by government and outside scientists to be sure any concerns are rapidly addressed.
- While background rates tell us that we cannot jump to conclusions or assume that any vaccine caused a particular health event, CDC takes every single adverse event report seriously and individually reviews all reports of serious adverse events so that potential problems can be quickly detected and investigated.

Background Rate Examples

- Guillain-Barré syndrome
 - In the normal course of time, out of 10 million Americans, approximately four will be diagnosed with Guillain-Barré syndrome in any given week.
 - If those same 10 million people were vaccinated on the same day, we would still expect to see about four reports of GBS the following week, and these cases would likely be coincidental, or unrelated, to the vaccine.
 - Despite this, each case would be investigated thoroughly to determine if the case could have been caused by the vaccine.
- Miscarriages:
 - Research shows that in the normal course of time, about 400 of every million pregnant women miscarry every day for various reasons.

- If those million women are vaccinated against 2009 H1N1 influenza today, we would expect that about 400 women would miscarry tomorrow, and those miscarriages would likely not be associated with the vaccine.